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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,389	10/07/2003	John H. Kenten	IGN-2005US02	7446

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EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

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09/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/681,389	KENTEN ET AL.	
	Examiner	Art Unit	
	Ileana Popa	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89 and 945-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office action.

2. Claims 1-79 and 81-93 have been cancelled. Claims 80 and 94 have been amended.

Claims 89 and 945-101 are pending and under examination.

Response to Arguments

Claim Rejections - 35 USC § 112, 2nd paragraph

3. The rejection of claims 80 and 94 under 35 U.S.C. 112, second paragraph, as being indefinite, is withdrawn in response to Applicant's amendments to the claims filed on 06/25/2007.

Claim Rejections - 35 USC § 112, new matter

4. The rejection of claim 94 under 35 U.S.C. 112, first paragraph, as introducing new matter, is withdrawn in response to Applicant's amendments to the claim filed on 06/25/2007.

Claim Rejections - 35 USC § 102

5. The rejection of claims 80 and 101 under 35 U.S.C. 102(e) as being anticipated by Johnston et al. (U.S. Patent No. 5,703,057, of record) is withdrawn in response to Applicant's amendments to the claims filed on 06/25/2007.

Claim Rejections - 35 USC § 103

6. The rejection of claims 80, 94-97, and 99-101 under 35 U.S.C. 103(a) as being unpatentable over Johnston et al., in view of each Ferro et al. (Eur J Cancer, 1997, 33: 1468-1478), Tang et al. (Nature, 1992, 356: 152-154, of record), and Sacca (Cardiovascular Research, 1997, 36: 3-9) is withdrawn in response to Applicant's amendments to the claims filed on 06/25/2007.

7. The rejection of claims 80, 94, 98, 100, and 101 under 35 U.S.C. 103(a) as being unpatentable over Johnston et al., in view of both Hohlfeld (Multiple Sclerosis, 1996, 1: 376-378) and Tang et al. is withdrawn in response to Applicant's amendments to the claims filed on 06/25/2007.

New Rejections

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees.

A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a

nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 80 and 94-101 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 and 7-16 of U.S. Patent No. 6,660,721. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are obvious variants.

The instant claim 80 is drawn to a method of stimulating an immune response directed to a heat shock fusion protein by administering to an animal a DNA construct encoding a fusion protein comprising (i) a heat shock protein fused to an epitope-containing segment, wherein the epitope-containing segment comprises two or more identical epitopes, (ii) a heat shock protein fused to two or more non-contiguous epitope-containing segments, each segment comprising one or more epitopes identical to the epitopes of the other segment(s), (iii) a heat shock protein fused to an epitope-containing segment comprising two or more identical or non-identical epitopes, wherein the segment is fused to the N-terminus or to an internal site of the heat shock protein, or (iv) a heat shock protein fused to an epitope-containing segment comprising one or more identical or non-identical epitopes, wherein the segment is fused to the N-terminus of the heat shock protein; claim 101 discloses that the fusion protein is ubiquitin. The instant claim 94 is drawn to a method of reducing the levels of a predetermined protein in an animal by using the above fusion protein, wherein the fusion protein comprises at

least one epitope from the predetermined protein; the predetermined protein is a male- or female-specific peptide hormone, such as gonadotropin releasing hormone (claims 95-97), tumor necrosis factor (claim 98), or growth hormone (claim 99); the fusion protein is further conjugated to a non-ubiquitin carrier protein (claim 101).

The patent claims 1-4 recite a method for stimulating an immune response directed to an ubiquitin fusion protein by administering to an animal an ubiquitin fusion protein comprising (i) a heat shock protein fused to an epitope-containing segment, wherein the epitope-containing segment comprises two or more identical epitopes (claim 1), (ii) a heat shock protein fused to two or more non-contiguous epitope-containing segments, each segment comprising one or more epitopes identical to the epitopes of the other segment(s) (claim 2), (iii) a heat shock protein fused to an epitope-containing segment comprising two or more identical or non-identical epitopes, wherein the segment is fused to the N-terminus or to an internal site of the heat shock protein (claim 3), or (iv) a heat shock protein fused to an epitope-containing segment comprising one or more identical or non-identical epitopes, wherein the segment is fused to the N-terminus of the heat shock protein (claim 4). The patent claims 7-10 recite a method for reducing the levels of a predetermined protein by using the above fusion proteins; the predetermined protein is a male- or female-specific peptide hormone, such as gonadotropin releasing hormone (claims 11-13), tumor necrosis factor (claim 14), or growth hormone (claim 15); the fusion protein is further conjugated to a non-ubiquitin carrier protein (claim 16). The patent claims do not recite administering a DNA encoding for the fusion proteins. However, one way of

administering the fusion protein is by providing the encoding DNA, wherein the fusion protein is expressed and elicits the immune response. Therefore, the patent claims disclose a method of simulating an immune response and a method of reducing the levels of a predetermined protein by providing an ubiquitin fusion protein. Thus, the patent claims 1-4 and 7-16 anticipate the instant claims 80 and 94-101. Since the claims of the U.S. Patent No. 6,660,721 embrace all limitation of the instant claims, the patent claims and the instant claims are obvious variants of one another.

It is noted that, although the instant application claims priority to the U.S. Patent No. 6,660,721 as being its divisional, no restriction is on file for the '721 patent.

Claim Rejections - 35 USC § 112, 2nd paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

11. Claims 80 and 94 recite the limitation of "the antibody to be detected". There is insufficient antecedent basis for this limitation in the claims.

Claims 95-101 are rejected for being dependent from the rejected claims 80 and 94 and also for failing to further clarify the basis of the rejection.

Claim Rejections - 35 USC § 112, new matter

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 89 and 945-101 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Specifically, the amendment to the claim to include non-contiguous epitope-containing segments each comprising "one or more epitopes identical to the epitopes of the other non-contiguos epitope-containing segments" is considered new matter. A search of the specification failed to provide literal support for the recitation of "one or more epitopes identical to the epitopes of the other non-contiguos epitope-containing segments"; the specification only provides support for non-contiguous epitope-containing segments, each comprising one or more identical or non-identical epitopes, i.e., identical epitopes are within each segment and not shared by the non-contiguous epitope-containing segments.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or

terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 80 and 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dalum et al. (J Immunol, 1996, 1545: 4796-4804), in view of both Kierrulf et al. (Mol Immunol, June, 1997, 34: 599-608, Abstract) and Tang et al. (Nature, 1992, 356: 152-154, of record).

Dalum et al. teach a method of stimulating an immune response directed to a fusion protein by administering to mice a fusion protein comprising ubiquitin (i.e., a heat shock protein) fused to an epitope-containing segment comprising one OVA epitope, wherein the epitope-containing segment is fused to an internal fusion site (claims 80

and 101) (Abstract, p. 4796, column 2, p. 4799, column 1 bridging column 2, p. 4801, column 1 bridging column 2). Dalum et al. do not teach an epitope-containing segment comprising two or more identical epitopes (claim 80). Kierrulf et al. teach that incorporating multiple copies of the same epitope enhances immunogenicity of the fusion proteins (claim 80) (Abstract). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the fusion protein of Dalum et al. by incorporating two or more copies of OVA epitopes, with a reasonable expectation of success. One of skill in the art would have been motivated to do so because Kierrulf et al. teach that fusion protein comprising more copies of the same epitope are more immunogenic. One of skill in the art would have been expected to have a reasonable expectation of success in making and using such a composition because the art teaches that such compositions can be successfully obtained and used. Dalum et al. taken with Kierrulf et al. do not teach a DNA vaccine (claim 80). Tang et al. teach DNA vaccines as being able to produce efficient immune responses (Abstract, p. 152, column 2 bridging p. 153). It would have been obvious to one of skill in the art, at the time the invention was made, to further modify the method of Dalum et al. and Kierrulf et al., by using a DNA vaccine to elicit an immune response to their fusion protein, with a reasonable expectation of success. The motivation to use a DNA and not a protein vaccine is provided by Tang et al., who teach that the use of a DNA vaccine is simple and shorten the time required to produce antibodies by eliminating the steps of protein purification and adjuvant administration (Abstract, p. 154, column 1 bridging column 2). One of skill in the art would have been expected to have a reasonable expectation of

success in making and using such because the art teaches the successful use of DNA vaccines to elicit immune responses. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

16. Claims 80, 94-97, 100, and 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dalum et al. taken with Kierrulf et al. and Tang et al., in further view of each Ferro et al. (Eur J Cancer, 1997, 33: 1468-1478, of record), Sacca (Cardiovascular Research, 1997, 36: 3-9, of record), and Johnston et al.

The teachings of Dalum et al., Kierrulf et al., and Tang et al. are applied as above for claims 80 and 101. Dalum et al., Kierrulf et al., and Tang et al. do not teach neutralizing the biological function of a predetermined protein by immunizing the animals with the ubiquitin fusion protein (claim 94), wherein the predetermined protein is gonadotropin releasing hormone (GnRH) (claims 95-97) or a growth hormone (claim 99). Ferro et al. teach the immunoneutralization of GnRH for immunocastration and as a potential anti-tumor treatment (claims 94-97) (Abstract, p. 1475, column 1, p. 1477, column 2). With respect to neutralization of growth hormone (claim 99), it is noted that Tang et al. teach DNA vaccines as being able to produce an efficient immune response against the human growth hormone (hGH) (Abstract, p. 152, column 2 bridging p. 153). It would have been obvious to one of skill in the art, at the time the invention was made, to use the method of Dalum et al., Kierrulf et al., and Tang et al. to make a DNA vaccine encoding a fusion ubiquitin-GnRH or ubiquitin-hGH, with a reasonable expectation of success. The motivation to use an anti-GnRh vaccine is provided by Ferro et al. who

teach the utility of immunoneutralizing GnRH for lowering the estradiol levels and therefore as a potential therapy in estrogen-sensitive disorders such as polycystic ovary syndrome and hormone-dependent breast cancer (p. 1468, column 1 bridging column 2). Additionally, one of skill in the art would have been motivated to immunoneutralize hGH because the art prior teaches that an excess of hGH is associated with certain diseases, such as acromegaly (see Sacca, p. 4, column 1 and 2). One of skill in the art would have been expected to have a reasonable expectation of success because the art teaches the successful use of DNA constructs encoding ubiquitin fusion proteins to elicit antibody responses in animals. It is noted that the limitation of the fusion protein being conjugated to a non-ubiquitin carrier protein (claim 100) is not innovative over the prior art. For example, Johnston et al. teach conjugation of ubiquitin fusion proteins with non-ubiqiuitin carrier proteins, such as KLH or BSA, to increase the immunogenicty of ubiquitin fusion proteins (claim 100) (column 24, lines 44-55). Therefore, one of skill in the art would have known and would have been motivated to further modify the ubiquitin fusion proteins according to the teachings of Johnston et al. to increase their immunogenicity. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

17. Claims 80, 98, and 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dalum et al. taken with Kierrulf et al. and Tang et al., in further view Hohlfeld (Multiple Sclerosis, 1996, 1: 376-378, of record).

The teachings of Dalum et al., Kierrulf et al., and Tang et al. are applied as above for claims 80 and 101. Dalum et al., Kierrulf et al., and Tang et al. do not teach neutralizing the biological function of tumor necrosis factor (TNF) (claims 94 and 98). Hohlfeld teaches the use of antibodies to inhibit TNF-α activity as a treatment for multiple sclerosis (Abstract, p. 377, column 1 bridging column 2). It would have been obvious to one of skill in the art, at the time the invention was made, to use the method of Dalum et al., Kierrulf et al., and Tang et al. to make a DNA vaccine encoding a fusion ubiquitin-TNF-α, with a reasonable expectation of success. The motivation to use an anti- TNF-α vaccine is provided by Hohlfeld who teaches the utility of immunoneutralizing TNF-α activity for the treatment of diseases such as multiple sclerosis and rheumatoid arthritis (p. 377, column 1 bridging column 2). One of skill in the art would have been expected to have a reasonable expectation of success because the art teaches the successful use of DNA constructs encoding ubiquitin fusion proteins to elicit antibody responses in animals. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

18. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

/Joseph Woitach/

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